REMARKS

At the outset, in the Advisory Action of April 9, 2009, the Examiner indicated that claims 1 and 18 are identical and because of a double patenting issue that arises, entry of the amendments to the claims cannot be made. In response, claim 1 has been amended to recite "consisting essentially of", which distinguishes claim 1 from claim 18. Therefore, double patenting issue fails to arise as a result of the amendments to the claims submitted herewith.

Below is a re-submission, identical to the comments submitted in the Response of April 3, 2009.

Claims 1, 8, 10, 11, 13 and 18 are pending in the application. The various amendments to claim 1 were made merely to conform with formal matters and to further clarify the claimed invention. Support for the newly added claim 18 can be found at least in Fig.1 of the present application. Newly added claim 18 indicates that genes coding for FSH beta and FSH alpha subunits be set forth sequentially in the 5' to 3' direction.

No new matter has been introduced. It is believed that no new issue has been raised requiring further search or consideration, particularly with regard to newly added claim 18 because the order of the FSH beta and FSHalpha subunits in the vector would have been already searched and considered during the prosecution of this application. Accordingly, entry of the amendments to the claims is respectfully requested.

Formalities

The Examiner has objected to the drawings/figures under 37 C.F.R. §§1.58(a) and 1.83 allegedly for inappropriate duplication of sequence listings. Applicants respectfully request that this objection be held in abeyance until the application is otherwise in condition for allowance. At which time Applicants will make the necessary revisions to the drawings/figures.

Rejection Under 35 U.S.C. §103

Claims 1, 8, 11, 13 and 17 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,674,711 in view of U.S. Application No. 2003144189, U.S. Patent 6,632,637, U.S. Patent 6,136,536, U.S. Application No. 20030083242, U.S. 6,852,510

and further in view of Logan et al. (Proc. Natl. Acad. Sci. USA, 1984, 81:3655-3659) and WO03/048366. Applicants traverse this rejection. Reconsideration and withdrawal of this rejection are respectfully requested.

At the outset, Applicants note that eight (8) references were cited in formulating this rejection.

Newly added claim 18 encompasses a vector comprising a gene encoding human FSH beta subunit, internal ribosomal entry site (IRES) sequence, and a gene encoding human FSH alpha subunit, sequentially in the 5' to 3' direction.

Lack of prima facie obviousness of the claimed invention - No reasonable expectation of success

US 6,632,637 (the '637 patent) discloses an expression vector that expresses at least two exogenous genes separated by an internal ribosomal entry site (IRES). The second coding sequences are those encoding selectable markers such as dihydrofolate reductase. The level of expression of these selectable marker genes was not of any concern in the reference, and as a result, the level of expression of the second gene was not quantitatively studied compared to the first coding sequence. In this regard, the '637 patent fails to disclose or suggest including a second "structural" protein related to the first polypeptide component for which quantitation and relative abundance of expression of the two related genes is desired to be understood. Moreover, the '637 patent fails to disclose or suggest the claimed (FSHbeta)(IRES)(FSHalpha) construct and its use for making a functional human FSH.

US 5,674,711 (the '711 patent) discloses that full biological activity of human FSH requires one to one stoichiometry of the alpha and beta subunits, as the Examiner has already noted (page 9, line 3-4, Final Office Action mailed February 3, 2009).

Given the combination of the above-cited references, a person of ordinary skill in the art would not have been motivated to use the (FSHbeta)(IRES)(FSHalpha) gene construct to make a full FSH protein for which a 1:1 stoichiometry of the subunits is desired with a reasonable expectation of success. While it may have been obvious to try to express the full FSH protein using the (FSHbeta)(IRES)(FSHalpha) construct, it cannot be overlooked that the '637 patent fails to provide evidence that a one-to-one expression of each of the two subunit polypeptides was produced from the vector. In the absence of such evidence, and in

view of the requirement that FSH protein formation be based on the presence of a one to one stoichiometry of it subunits, Applicants assert that the Examiner has failed to meet the burden of establishing *prima facie* obviousness of the claimed invention for the (FSHbeta)(IRES)(FSHalpha) vector construct for expressing human FSH. Accordingly, the presently claimed invention is not obvious over the cited references.

Teaching Away

In addition to the above reasons why the presently claimed invention is not obvious over the cited documents, the Examiner's attention is directed to Mizuguchi et al., "IRES-Dependent Second Gene Expression Is Significantly Lower Than Cap-Dependent First Gene Expression in a Bicistronic Vector", Molecular Therapy, Vol. 1, No. 4, April 2000, pages 376-382 (enclosed herewith), which teaches away from the claimed invention. Miguchi discloses that the expression of the IRES-dependent second gene was less efficient than that of the first gene under both *in vitro* and *in vivo* conditions, as the title suggests. See also page 379, column 1, lines 12-15.

In view of the fact that Miguchi discloses that the level of expression of the second gene product was lower than expression of the first gene product, a person of ordinary skill in the art attempting to make human FSH protein would be dissuaded from making the (FSHbeta)(IRES)(FSHalpha) construct to express the FSH protein, because a one to one stoichiometry of the polypeptide subunits expressed from the (FSHbeta)(IRES)(FSHalpha) construct obviously could not be achieved. A person of ordinary skill in the art of making human FSH protein would search for a vector that expresses both FSHbeta and FSHalpha at about the same level so that the full FSH protein can be made efficiently. In contrast to the Miguchi disclosure, the present application describes a surprising discovery that a full FSH protein can be made efficiently, and that the (FSHbeta)(IRES)(FSHalpha) construct produces one to one stoichiometry of the subunits. Therefore, the presently claimed invention is not obvious over the cited references.

Allowable Subject Matter

Applicant acknowledges the Examiner's indication that the subject matter of claim 10 is in allowable condition.

Conclusion

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to JHK Law's Deposit Account No. **502486** during the pendency of prosecution of this application. Should such additional fees be associated with an extension of time, applicant respectfully requests that this paper be considered a petition therefor.

Respectfully submitted,

JHK Law

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